AMENDMENTS TO THE CLAIMS

Claims 1-16 (Cancelled)

16. (Currently Amended) A method of site-specific downregulation of connexin protein expression for a therapeutic or a cosmetic purpose which comprises administering at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to a site on or within a patient at which said downregulation is required.

17. (Currently Amended) A method of reducing neuronal cell death which would otherwise result from a neuronal insult to a specific site in the brain, spinal cord or optic nerve of a patient which comprises the step of administering at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to said site to downregulate expression of a connexin protein at and immediately adjacent said site.

18. (Currently Amended) A method according to claim 17 in which said anti-sense polynucleotide ~~the formulation~~ is administered to reduce neuronal loss due to physical trauma to the brain, spinal cord or optic nerve.

19. (Currently Amended) A method according to claim 17 in which said anti-sense polynucleotide ~~the formulation~~ is administered in a sufficient amount to downregulate expression of said connexin protein for at least 24 hours post-administration.

20. (Currently Amended) A method of promoting wound healing in a patient which comprises the step of administering at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to said wound to downregulate expression of a connexin protein at and immediately adjacent the site of said wound.

21. (Original) A method according to claim 20 in which the wound is the result of trauma.

22. (Original) A method according to claim 21 in which the trauma is a burn.

23. (Original) A method according to claim 20 in which the wound is the result of a surgery.

24. (Currently Amended) A method of reducing inflammation as part of treating a wound or a tissue subjected to a physical trauma which comprises the step of administering at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to, or proximate to, said wound or tissue.

25. (Currently Amended) A method according to claim 24 in which said anti-sense polynucleotide [the formulation] is administered to reduce inflammation due to physical trauma to the brain, spinal cord or optic nerve.

26. (Currently Amended) A method of decreasing scar formation in a patient who has suffered a wound which comprises the step of administering at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to said wound to downregulate expression of a connexin protein at and immediately adjacent the site of said wound.

27. (Currently Amended) A method of skin rejuvenation or thickening for a cosmetic or therapeutic purpose which comprises the step of administering, once or repeatedly, at least one anti-sense polynucleotide to a connexin protein ~~a formulation as defined in claim 1~~ to a skin surface.

28. (Currently Amended) A method according to claim 27 wherein said anti-sense [formulation includes] polynucleotide is

directed to connexin 43 and is administered to regulate epithelial basal cell division and growth.

29. (Currently Amended) A method according to claim 27 wherein said anti-sense [formulation includes] polynucleotide is directed to connexin 31.1 and is administered to regulate outer layer keratinisation.

30. (Currently Amended) A method according to claim 27 wherein said anti-sense polynucleotide [the formulation] is in a cream.

Claims 31-42 (Cancelled)

43. (New) A method according to claim 16, wherein said anti-sense polynucleotide is an oligodeoxynucleotide.

44. (New) A method according to claim 16, wherein said connexin protein is selected from the group consisting of connexin 43, connexin 26, connexin 31.1, connexin 32 and connexin 36.

45. (New) A method according to claim 16, wherein said anti-sense polynucleotide is present in a formulation together with a pharmaceutically acceptable carrier or vehicle.

46. (New) A methodaccording to claim 45, wherein said formulation is suitable for topical administration.

47. (New) A method according to claim 45, wherein said formulation contains polynucleotides to one connexin protein only.

48. (New) A method according to claim 45, wherein said formulation contains polynucleotides to more than one connexin protein.

49. (New) A method according to claim 48, in which one of the connexin proteins to which polynucleotides are directed is connexin 43.

50. (New) A method according to claim 48, which includes polynucleotides directed to at least two of connexin 26, connexin 31.1, connexin 32, connexin 36 and connexin 43.

51. (New) A method according to claim 45, wherein the pharmaceutically acceptable carrier or vehicle is, or includes, a gel.

52. (New) A method according to claim 51 in which the gel is a nonionic polyoxyethylene-polyoxypropylene copolymer gel.

53. (New) A method according to claim 45, wherein the formulation further includes a surfactant or urea to assist with polynucleotide penetration into a cell.

Claims 16-30, and claims 43-53 are currently pending in this application. Claims 16-20, and 24-30 have been amended. Claims 31-42 have been cancelled. Claims 43-53 have been added. Support for the amendments to claims 16-20, and 24-30 may be found in original claim 1. Support for new claims 43-53 may be found in original claims 1-15.

The Examiner has required restriction between Groups I-XIII. Applicants respectfully traverse the restriction requirement, and provisionally elect Group VII.

The Commissioner may require restriction if two or more independent and distinct inventions are claimed in a single application (37 CFR 1.142(a)). In the present case, although the claimed subject matter may be classified in different classes, the inventions are not independent.

The Examiner has indicated that claim 16 links inventions VI-IX and that upon allowance of claim 16, the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of claim 16 will be entitled to examination in the instant application.

Claim 16 is novel and inventive over all the prior art documents cited in the International Preliminary Examination Report. None of cited references disclose a method of therapeutic or cosmetic treatment involving administering a connexin antisense polynucleotide. In particular, Ruch *et al.* describes an *in vitro* study looking at how changes in cell coupling affect the growth rate of BALB/c3T3 cells in culture. Goliger *et al.* describes an *in vitro* study purely aimed at separating conductances of channels composed of connexins 43 and 40 is order to identify which conductances are related to which connexin types. WO 98/24797A reports an *in vitro* study to examine the effect of connexin 43 anti-sense oligonucleotides on progesterone secretion by bovine luteal cells. There is no teaching or suggestion in any of Ruch *et al.*, Goliger *et al.*, WO 98/24797A, Moore *et al.* or Grazul-Bilska *et al.*, of using anti-sense connexin oligonucleotides in treating a patent for either therapeutic or cosmetic purposes. Claim 16 is thus novel and inventive over the prior art cited during International Preliminary Examination.

The claims have been amended so that the claims are all directed to methods which include all the limitations of claim 16. Accordingly, the Examiner is requested to examine all of the new claims, which are directed to linked inventions VI-IX.

It is respectfully requested that the restriction requirement be withdrawn, and that each of claims 16-30, and 43-53 presently pending in this application be examined.

Enclosed is a petition for a two month extension of time and a check for $420. Applicant believes no additional fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 06-2375, under Order No. HO-P02246US0 from which the undersigned is authorized to draw.

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Respectfully submitted,

By _____

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